DISCUSSION OF THE AMENDMENT

A typographical error has been corrected in the specification.

Claim 36 has been cancelled. Each of Claims 37-68 have been amended to include a pharmaceutically acceptable carrier.

No new matter has been added by the above amendment. Claims 1-35 and 37-68 are now pending in the application.

REMARKS

The present invention is drawn to penem compounds having a cis configuration, and substituted at the six-position with a 1-hydroxypropyl group. The present compounds thus have a (1'S, 5R, 6R) configuration, which is equivalent to a (5R, 6R, 8S) configuration. The claimed compounds are particularly effective against methicillin-resistant *staphylococcus aureus* (MRSA) as disclosed in the specification in the paragraph bridging pages 2 and 3.

As further disclosed at pages 2-3 of the specification, analogous compounds containing a 1-hydroxyethyl group as a 6-position substituent have insufficient activities compared with those having a (1'R, 5R, 6S) configuration. Moreover, it is also known that if the steric configuration of the 6-position hydroxyalkyl group is (1'R, 5R, 6S), compounds containing a propyl or a higher alkyl group as the alkyl group are no longer equipped with any substantial activity. Therefore, the art has primarily investigated substitution at the 2-position for the improvement of activities of penem compounds. Thus, against the above background, it was surprising and unexpected that the presently-claimed compounds possessed the asserted activity.

The rejection of Claims 1, 33, 36 and 37 under 35 U.S.C. §103(a) as unpatentable over

U.S. 4,540,579 to Afonso et al, is respectfully traversed. Afonso et al is no better than the above-discussed prior art, and indeed Afonso et al direct persons skilled in the art to the (5R, 6S, 8R) configuration and 1-hydroxyethyl as the 6-substituent. Applicants recognize that Afonso et al does disclose cis isomers within their broad disclosure, such as at column 2, line 20. However, the statute requires that the subject matter as a whole must be considered. One skilled in the art would not consider Afonso et al in a vacuum, but would bring to the consideration all prior art knowledge in this field. Armed with such knowledge, one skilled in the art would not be led to the presently claimed compounds. Accordingly, it is respectfully requested that the rejection over Afonso et al be withdrawn.

The rejection of Claims 1, 17-19, 32-34, 36, 37 and 54-56 under 35 U.S.C. §103(a) over the literature reference "Synthesis of Optically Active Penems" (Girijavallabhan et al) is respectfully traversed. Girijavallabhan et al is deficient for substantially the same reasons as Afonso et al, which reasons are hereby incorporated by reference. While compound (23) of Girijavallabhan et al does have a (1'S, 5R, 6R) configuration, that compound contains a 1-hydroxyethyl group. Accordingly, it is respectfully requested that the rejection over Girijavallabhan et al be withdrawn.

The rejection of Claims 1-34, and 36-68 under 35 U.S.C. §103(a) as unpatentable over JP 4-69387 to Ishiguro et al, is respectfully traversed. Ishiguro et al relates to a process for the preparation of cis-form penems by irradiation with light. The relevant disclosure of Ishiguro et al is no more relevant than that of the other prior art references discussed above. Again, there is no direction in Ishiguro et al to make a 1-hydroxypropyl-substituted compound at the 6-position for a (5R, 6R, 8S) penem. Accordingly, it is respectfully requested that the rejection over Ishiguro et al be withdrawn.

The rejection of Claims 1-4, 7-19, 31-34, 36-57, 60, 63 and 66-68 under U.S. 4,742,052 to Sunagawa et al, is respectfully traversed. Again, and as discussed above, Sunagawa et al is no more relevant than the above-described prior art, since the only disclosure of (5R, 6R, 8S) compounds are those substituted at the 6-position with 1-hydroxyethyl. Moreover, why would one skilled in the art be led to the (5R, 6R, 8S) configuration, when Sunagawa et al disclose that the (5R, 6R, 8R) and (5R, 6S, 8R) configurations are most preferred? Accordingly, it is respectfully requested that the rejection over Sunagawa et al be withdrawn.

The rejection of Claims 1, 30, 31, 33, 36, 37, 66, and 67 under 35 U.S.C. §103(a) as unpatentable over U.S. 4,272,437 to Menard et al, is respectfully traversed. While Menard et al disclose broadly hydroxy-substituted lower alkyl groups at the 6-position, 1-hydroxyethyl is disclosed as preferred, as is the (1'R, 5R, 6S) and (1'S, 5S, 6R) disclosed as preferred. Clearly, Menard et al directs one skilled in the art away from the presently-claimed compounds. Menard et al is deficient for essentially the same reasons as the above-discussed prior art. Accordingly, it is respectfully requested that the rejection over Menard et al be withdrawn.

The rejection of Claims 1-34, and 36-68 under 35 U.S.C. §103(a) as unpatentable over U.S. 4,692,442 to Gosteli et al, is respectfully traversed. While Gosteli et al do disclose 1-hydroxypropyl, among other substituent groups at the 6-position, there is no direction in Gosteli et al to use the (5R, 6R, 8S) configuration. Indeed, all of the production process and working examples therein are drawn to other, such as the trans, configurations. Again, there is no direction in Gosteli et al to make the present compounds. Accordingly, it is respectfully requested that the rejection over Gosteli et al be withdrawn.

The rejection of Claims 1-32, and 36-68 under 35 U.S.C. §103(a) as unpatentable over U.S. 4,748,162 over Leanza et al, is respectfully traversed. While Leanza et al disclose individually a 1-hydroxypropyl at the 6-position and the 5R, 6R cis isomer, the reference does not disclose the two in combination. Example 4 thereof, relied on by the Examiner, contains a 2-hydroxy-2-propyl group as the 6-substituent, not the presently-required 1-hydroxypropyl group. Moreover, in column 20 wherein relationships between steric configurations and 6-substituents are disclosed, it is only the trans-form compound (lines 13-20) that contains 1-hydroxypropyl as a preferred 6-substituent, and 1-hydroxypropyl is not included in preferred illustrative 6-substituents for cis forms. For all of the above reasons, it is respectfully requested that the rejection over Leanza et al be withdrawn.

The rejection of Claims 1, and 36-40 under 35 U.S.C. §102(b) as anticipated by, and of Claims 1, 33, and 36-40 under 35 U.S.C. §103(a) as unpatentable over, EP 0069373 to Minamida et al, is respectfully traversed. The Examiner asserts that Minamida et al disclose the racemate of the presently claimed compounds. However, a racemate does not anticipate the compound, because the compounds are not claimed in combination with their enantiomer. Nor would it have been obvious to separate the 1'S from the 1'R enantiomer. Nor does it appear that any 1-hydroxypropyl compound substituted at the 6-position were actually synthesized in Minamida et al. Accordingly, it is respectfully requested that the rejections over Minamida et al be withdrawn.

The rejection of Claim 35 under 35 U.S.C. §103(a) as unpatentable over either Girijavallabhan et al or Gosteli et al, is respectfully traversed, for substantially the same reasons as discussed above with regard to the above two references. Accordingly, it is respectfully requested that these rejections be withdrawn.

The rejection of Claims 38-68 under 35 U.S.C. §112, second paragraph, is respectfully traversed to the extent it applies to the claims as amended. Indeed, the rejection is now moot. Accordingly, it is respectfully requested that it be withdrawn.

In view of the cancellation of Claim 36, there is no longer an objection with regard to Claims 36 and 37. Accordingly, it is respectfully requested that the objection be withdrawn.

All of the presently pending claims in this application are now believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to Issue.

Respectfully submitted,

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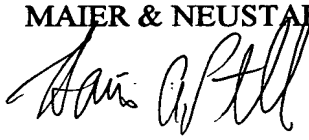

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